



## WE CLAIM:

1. (Amended) A method of administering a glucagon-like peptide-1 (GLP-1) molecule having the amino acid sequence of SEQ ID NO: 1:

R<sub>1</sub>-X-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Val-Ser-Ser-Tyr-  
Leu-Y-Gly-Gln-Ala-Ala-Lys-Z-Phe-Ile-Ala-Trp-Leu-Val-  
Lys-Gly-Arg-R<sub>2</sub> (SEQ ID NO:1)

wherein:

R<sub>1</sub> is histidine;

X is Gly, Val, Thr, Ile, or alpha-methyl-Ala;

Y and Z are each Glu; and

R<sub>2</sub> is NH<sub>2</sub> or Gly-OH;

said method comprising the step of administering an effective amount of the GLP-1 molecule, or a pharmaceutically-acceptable salt of the GLP-1 molecule, to a patient in need thereof by pulmonary means.

2. (Amended) The method of **Claim 1**, wherein the GLP-1 molecule is delivered to lower airways of the patient.

3. The method of **Claim 2**, wherein the GLP-1 molecule is deposited in the alveoli.

4. The method of **Claim 1**, wherein the GLP-1 molecule is inhaled through the mouth of the patient.

5. The method of **Claim 1**, wherein the GLP-1 molecule is administered as a pharmaceutical formulation comprising the GLP-1 molecule in a pharmaceutically acceptable carrier.

6. The method of **Claim 5**, wherein the formulation is selected from the group consisting of a solution in an aqueous medium and a suspension in a non-aqueous medium.

7. The method of **Claim 6**, wherein the formulation is administered as an aerosol.

8. The method of **Claim 5**, wherein the formulation is in the form of a dry powder.

9. The method of **Claim 5**, wherein the GLP-1 molecule has a particle size of less than about 10 microns MMAD.

10. The method of **Claim 9**, wherein the GLP-1 molecule has a particle size of about 1 to about 5 microns MMAD.

11. The method of **Claim 10**, wherein the GLP-1 molecule has a particle size of about 2 to about 3 microns MMAD.

12. The method of **Claim 1**, wherein at least about 10% of the GLP-1 molecule delivered is deposited in the lung.

13. The method of **Claim 1**, wherein the GLP-1 molecule is delivered from an inhalation device suitable for pulmonary administration and capable of depositing the GLP-1 molecule in the lungs of the patient.

14. The method of **Claim 13**, wherein the device is selected from the group consisting of a nebulizer, a metered-dose inhaler, a dry powder inhaler, and a sprayer.

15. The method of **Claim 14**, wherein the device is a dry powder inhaler.

18. (Amended) A method of administering Val<sup>8</sup>-GLP-1(7-37)OH, Gly<sup>8</sup>-GLP-1(7-37)OH or Asp<sup>8</sup>-GLP-1(7-37)OH, comprising administering an effective amount of Val<sup>8</sup>-GLP-1(7-37)OH, Gly<sup>8</sup>-GLP-1(7-37)OH or Asp<sup>8</sup>-GLP-1(7-37)OH or a pharmaceutically acceptable salt thereof, to a patient in need thereof by pulmonary means.

19. (Amended) A method of administering Val<sup>8</sup>-GLP-1(7-37)OH, comprising administering an effective amount of Val<sup>8</sup>-GLP-1(7-37)OH, or a pharmaceutically acceptable salt of Val<sup>8</sup>-GLP-1(7-37)OH, to a patient in need thereof by pulmonary means.

21. (Amended) A method for treating a patient with diabetes, comprising administering an effective dose of a GLP-1 molecule, or a pharmaceutically acceptable salt of the GLP-1 molecule, to the patient by pulmonary means, said GLP-1 molecule having the amino acid sequence of SEQ ID NO: 1:

R<sub>1</sub>-X-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Val-Ser-Ser-Tyr-  
Leu-Y-Gly-Gln-Ala-Ala-Lys-Z-Phe-Ile-Ala-Trp-Leu-Val-  
Lys-Gly-Arg-R<sub>2</sub> (SEQ ID NO:1)

wherein:

R<sub>1</sub> is histidine;

X is Gly, Val, Thr, Ile, or alpha-methyl-Ala;

Y and Z are each Glu; and

R<sub>2</sub> is NH<sub>2</sub> or Gly-OH.

22. The method of **Claim 21**, wherein the GLP-1 molecule is administered as a pharmaceutical formulation comprising the GLP-1 molecule in a pharmaceutically acceptable carrier.

23. (Amended) A method for treating a patient with diabetes, comprising administering an effective dose of Val<sup>8</sup>-GLP-1(7-37)OH or a pharmaceutically effective salt of Val<sup>8</sup>-GLP-1(7-37)OH, to the patient by pulmonary means.

24. The method of **Claim 21**, wherein the GLP-1 molecule is Gly<sup>8</sup>-GLP-1(7-37)OH.

25. The method of **Claim 21**, wherein the GLP-1 molecule is delivered from an inhalation device suitable for pulmonary administration and capable of depositing the GLP-1 molecule in the lungs of the patient.

26. The method of **Claim 25**, wherein the device is a sprayer or a dry powder inhaler.

27. The method of **Claim 25**, wherein an actuation of the device administers about 40 µg to about 4,000 µg of a GLP-1 molecule.

28. The method of **Claim 25**, wherein an actuation of the device administers about 80 µg to about 2,000 µg of a GLP-1 molecule.

29. The method of **Claim 25**, wherein an actuation of the device administers about 160 µg to about 1,000 µg of a GLP-1 molecule.

30. The method of **Claim 25**, wherein an actuation of the device administers about 320 µg to about 500 µg of a GLP-1 molecule.

31. (Amended) A method for treating a patient with hyperglycemia comprising, administering an effective dose of a GLP-1 molecule, or a pharmaceutically acceptable salt of the GLP-1 molecule, to the patient by pulmonary means, said GLP-1 molecule having the amino acid sequence of SEQ ID NO: 1:

R<sub>1</sub>-X-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Val-Ser-Ser-Tyr-  
Leu-Y-Gly-Gln-Ala-Ala-Lys-Z-Phe-Ile-Ala-Trp-Leu-  
Val-Lys-Gly-Arg-R<sub>2</sub> (SEQ ID  
NO:1)

wherein:

R<sub>1</sub> is histidine;

X is Gly, Val, Thr, Ile, or alpha-methyl-Ala;

Y and Z are each Glu; and

R<sub>2</sub> is NH<sub>2</sub> or Gly-OH.

32. The method of **Claim 31**, wherein the GLP-1 molecule is administered as a pharmaceutical formulation comprising the GLP-1 molecule in a pharmaceutically acceptable carrier.

33. A method for treating a patient with hyperglycemia, comprising administering an effective dose of Val<sup>8</sup>-GLP-1(7-37)OH, or a pharmaceutically acceptable salt of Val<sup>8</sup>-GLP-1(7-37)OH, to the patient by pulmonary means.

34. The method of **Claim 31**, wherein the GLP-1 molecule is Gly<sup>8</sup>-GLP-1(7-37)OH.

35. The method of **Claim 31**, wherein the GLP-1 molecule is delivered from an inhalation device suitable for pulmonary administration and capable of depositing the GLP-1 molecule in the lungs of the patient.

36. The method of **Claim 35**, wherein the device is selected from the group consisting of a sprayer and a dry powder inhaler.

37. The method of **Claim 35**, wherein an actuation of the device administers about 40 µg to about 4,000 µg of GLP-1 molecule.

38. The method of **Claim 35**, wherein an actuation of the device administers about 80 µg to about 2,000 µg of the GLP-1 molecule.

39. The method of **Claim 35**, wherein an actuation of the device administers about 160 µg to about 1,000 µg of GLP-1 molecule.

40. The method of **Claim 35**, wherein an actuation of the device administers about 320 µg to about 500 µg of the GLP-1 molecule.

41. A method of administering a glucagon-like peptide-1 (GLP-1) molecule, said method comprising the step of administering an effective amount of the GLP-1 molecule, or a pharmaceutically acceptable salt of the GLP-1 molecule, to a patient in need thereof by pulmonary means, wherein said GLP-1 molecule has the amino acid sequence of GLP-1(7-34)OH, GLP-1(7-34)NH<sub>2</sub>, GLP-1(7-35)OH, GLP-1(7-35)NH<sub>2</sub>, GLP-1(7-36)OH, GLP-1(7-36)NH<sub>2</sub>, GLP-1(7-37)OH or GLP-1(7-37)NH<sub>2</sub>, modified by replacing alanine at position 8 with an amino acid having an uncharged side chain.

42. A method for treating a patient with diabetes, comprising administering an effective dose of a GLP-1 molecule, or a pharmaceutically effective salt of the GLP-1 molecule, to the patient by pulmonary means, wherein said GLP-1 molecule has the amino acid sequence of GLP-1(7-34)OH, GLP-1(7-34)NH<sub>2</sub>, GLP-1(7-35)OH, GLP-1(7-35)NH<sub>2</sub>, GLP-1(7-36)OH, GLP-1(7-36)NH<sub>2</sub>, GLP-1(7-37)OH or GLP-1(7-37)NH<sub>2</sub>, modified by replacing alanine at

position 8 with an amino acid having an uncharged side chain or the amide form thereof.

43. A method for treating a patient with hyperglycemia, comprising administering an effective dose of a GLP-1 molecule, or a pharmaceutically acceptable salt of the GLP-1 molecule, to the patient by pulmonary means, wherein said GLP-1 molecule has the amino acid sequence of GLP-1(7-34)OH, GLP-1(7-34)NH<sub>2</sub>, GLP-1(7-35)OH, GLP-1(7-35)NH<sub>2</sub>, GLP-1(7-36)OH, GLP-1(7-36)NH<sub>2</sub>, GLP-1(7-37)OH or GLP-1(7-37)NH<sub>2</sub>, modified by replacing alanine at position 8 with an amino acid residue having an uncharged side chain or the amide form thereof.